

29. (Previously presented) The array of claim 8, wherein the designate nucleotides and/or nucleotide analogs comprise a purine or pyrimidine base, a ribose or deoxyribose sugar, and a phosphate group.

#### REMARKS

Applicants appreciate Examiner's indication that claims 7, 8, 10-12, 23-26, 28 and 29 are in condition for allowance. In view of the lengthy prosecution to date, Applicants hereby cancel all rejected claims, claims 1-4, 6, 20-22 and 27, solely to expedite issuance of a patent. Cancellation of claims should not be interpreted as an acquiescence to the outstanding rejections. Applicants reserve the right to pursue similar claims in this or related applications.

#### Rejection of Claims 1, 3, 4, 20, 22 and 27 Under 35 U.S.C. 102 (b) and 103

The Examiner has rejected claims 1, 3, 4, 20, 22 and 27 as allegedly anticipated under 35 U.S.C. 102(b) by Candrian et al. (Applied and Environmental Microbiology (1991) April, pages 955-961).

The Examiner states, "Candrian et al. teach a primer comprising the following pattern of universal and designate nucleotides which meet the limitations of [claim 1]: 5' TTITTCTGTATTITCTTTTCHICTTTTITCAG 3'. Further, claims 3 and 4 are also anticipated...in that a plurality of instances of the pattern exists and designate nucleotides are bound to the end of the sequence."

The Examiner applies similar arguments to claims 20, 22 and 27.

The Examiner further rejects claims 1-4, 6, 20-22 and 27 under 35 U.S.C. 103(a) as being unpatentable over Candrian et al. in view of Bergstrom et al. (Nucleic Acid Research (1997) Vol. 25, pages 1935-1942).

The Examiner argues, "Candrian et al. teach the use of inosine-containing oligonucleotide primers for enzymatic amplification of different alleles...Candrian et al. do not teach the use of 5-nitroindole or 3-nitropyrrole nucleotide analogs. However, Bergstrom et al. do teach incorporation of these analogs into oligonucleotides. It would have been prima facie

obvious to one of ordinary skill in the art at the time of the invention to utilize 5-nitroindole and 3-nitropyrrole in the primers designed by Candrian et al.”

Applicants respectfully assert that Candrian et al. does not anticipate any of the claims of the present application. It is axiomatic that in order to anticipate a claim, a reference must disclose each and every element of the claimed subject matter, either explicitly or inherently. Here, all of the pending claims, including claims 1, 3, 4, 20, 22 and 27 contain a “universal” nucleotide or nucleotide analog. As understood in the specification and in the now-extensive prosecution record, the term “universal” refers to: “an entity (or collection of entities mutually substituted at a position) that is relatively non-specific with respect to all of A, T, C and G. Exemplary universal bases are 5-nitroindole and 3-nitropyrrole. As would be appreciated by one of skill in the art, any ‘universal’ base will have some heterogeneity in free energy of hybridization with different partners.” (see Applicants’ response dated Aug. 3, 2001).

Applicants submit that inosine is not a “universal” nucleotide. Inosine is known in the art to hybridize specifically with A and C but not with G or T. For example, see Macevitz et al. (WO 90/04652, previously cited in this prosecution) at page 4, line 16, which reads, “because deoxyinosine (I) forms nearly equally strong base pairs with A and C, but forms only a weak or destabilizing base pair with either G or T, deoxyinosine can replace G and T in a probe.” Accordingly, inosine cannot be considered to be a universal nucleotide as the term is used in this application. However, Applicants note that a degenerate position created by the use of a mixture of I, C and A at a single position in a probe would be equivalent to a universal nucleotide. Such a mixture is not suggested by Candrian et al.

Accordingly, Candrian et al. does not teach or suggest, explicitly or implicitly, the use of a probe containing a “universal” nucleotide and cannot, therefore, anticipate the present claims.

Furthermore, Applicants assert that there would have been no motivation to replace inosine in the probes of Candrian et al. with the universal nucleotides described in Bergstrom et al. Candrian et al. achieved sufficient degeneracy for their intended purpose (DNA amplification) by using inosine and would not have been motivated to seek nucleotides having greater degeneracy.

For these reasons, Applicants maintain that all of the present claims are novel and non-obvious with respect to Candrian et al. and with respect to Candrian et al. in view of Bergstrom et al.

Nonetheless, solely to expedite prosecution, all presently rejected claims are canceled, without prejudice. Therefore claims 1-4, 6, 20-22 and 27 are canceled, rendering all rejections moot.

#### CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Applicants hereby request that any fee required for timely consideration of this submission be charged to Deposit Account No. 18-1945.

Dated: September 3, 2004

Respectfully submitted,

By   
John D. Quisel

Registration No.: 47,874  
ROPES & GRAY LLP  
One International Place  
Boston, Massachusetts 02110-2624  
(617) 951-7000  
(617) 951-7050 (Fax)  
Attorneys/Agents For Applicant



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.                          | CONFIRMATION NO. |
|---|-------------|----------------------|--|------------------|
| 09/416,779  | 10/13/1999  | FRANCO P. PREPARATA  | <del>09/416,779</del><br><b>BURF-101-010</b> | 6623             |
| 28120   | 7590        | 08/20/2004           | EXAMINER                                     |                  |
| ROPE & GRAY LLP<br>ONE INTERNATIONAL PLACE<br>BOSTON, MA 02110-2624 |             |                      | CLOW, LORI A                                 |                  |
|   |             |                      | ART UNIT                                     | PAPER NUMBER     |
|   |             |                      | 1631   |                  |

Ropes & Gray

AUG 23 2004

Intellectual Property Dept.

DATE MAILED: 08/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Ropes & Gray**

**Symbol #:** BURF-101-010

**Action Due:** Response to Non-Compliant OA

**Deadline(s):** 20 Sep 2004 / 20 Feb 2005  
Final / Final w/ ext



UNITED STATES PATENT AND TRADEMARK OFFICE



09/4/6, 779

COMMISSIONER FOR PATENTS  
UNITED STATES PATENT AND TRADEMARK OFFICE  
P.O. BOX 1450  
ALEXANDRIA, VA 22313-1450  
WWW.USPTO.GOV

Office of Non-Compliant Amendment (37 CFR 1.121)

The amendment document filed on 8/9/04 is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121. In order for the amendment document to be compliant, correction of the following item(s) is required. Only the corrected section of the non-compliant amendment document must be resubmitted (in its entirety), e.g., the entire "Amendments to the claims" section of applicant's amendment document must be re-submitted. 37 CFR 1.121(h).

THE FOLLOWING CHECKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

- ☐ 1. Amendments to the specification:
- ☐ A. Amended paragraph(s) do not include markings.
  - ☐ B. New paragraph(s) should not be underlined.
  - ☐ C. Other \_\_\_\_\_
- ☐ 2. Abstract:
- ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
  - ☐ B. Other \_\_\_\_\_
- ☐ 3. Amendments to the drawings: \_\_\_\_\_
- ☒ 4. Amendments to the claims:
- ☐ A. A complete listing of all of the claims is not present.
  - ☐ B. The listing of claims does not include the text of all pending claims (including withdrawn claims)
  - ☒ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified. Note: the status of every claim must be indicated after its claim number by using one of the following 7 status identifiers: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New) and (Not entered).
  - ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
  - ☐ E. Other: \_\_\_\_\_

For further explanation of the amendment format required by 37 CFR 1.121, see MPEP Sec. 714 and the USPTO website at <http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/officesliver.pdf>.

If the non-compliant amendment is a **PRELIMINARY AMENDMENT**, applicant is given **ONE MONTH** from the mail date of this letter to supply the corrected section which complies with 37 CFR 1.121. Failure to comply with 37 CFR 1.121 will result in non-entry of the preliminary amendment and examination on the merits will commence without consideration of the proposed changes in the preliminary amendment(s). This notice is not an action under 35 U.S.C. 132, and this **ONE MONTH** time limit is not extendable.

If the non-compliant amendment is a reply to a **NON-FINAL OFFICE ACTION** (including a submission for an RCE), and since the amendment appears to be a *bona fide* attempt to be a reply (37 CFR 1.135(c)), applicant is given a **TIME PERIOD** of **ONE MONTH** from the mailing of this notice within which to re-submit the corrected section which complies with 37 CFR 1.121 in order to avoid abandonment. **EXTENSIONS OF THIS TIME PERIOD ARE AVAILABLE UNDER 37 CFR 1.136(a).**

If the amendment is a reply to a **FINAL REJECTION**, this form may be an attachment to an Advisory Action. The period for response to a final rejection continues to run from the date set in the final rejection, and is not affected by the non-compliant status of the amendment.

  
Legal Instruments Examiner (LIE)

571-272-0549  
Telephone No.